

On the Physiological Action of the Chinoline and Pyridine Bases.

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(Abstract.)

It is well known that quinine, cinchonine, or strychnine yield, when distilled with caustic potash, two homologous series of bases, named the pyridine and chinoline series. Bases isomeric with these may also be obtained by the destructive distillation of coal, or from Dippel's oil, got from bone. Greville Williams has pointed out that chinoline obtained from coal-tar differs in some respects from that yielded by cinchonine. In this research the authors endeavoured to ascertain (1) the physiological action of the various members of the series; (2) whether there was any difference in this respect between the members of the series obtained from cinchonine and those got from tar; and (3) whether, and if so, how, both as regards extent and character, the physiological action of these bases differed from that of the original alkaloidal bodies.

The bases in both series are difficult to separate from each other; but this has been done as far as possible by repeated fractional distillation. The salt employed was the hydrochlorate. This, dissolved in water, was introduced by a fine syringe under the skin of the animal. The action of chinoline was tested on frogs, mice, rabbits, guineapigs, cats, dogs, and man; but as the effects were found to be similar in all of these instances, the majority of the observations were made on rabbits. The experiments with the other substances were made on rabbits and frogs. The physiological action of hydrochlorate of chinoline was first examined. Its action was then compared with that of the hydrochlorates of the chinoline series of bases distilling at higher temperatures, including such as lepidine, dispoline, tetrahiroline, &c. In the next place, the physiological action of the pyridine series was studied, beginning with pyridine itself, and passing upwards to bases obtained at still higher boiling-points, such as picoline, lutidine, &c. Lastly, the investigation was directed to the action of condensed bases, such as dipyridine, parapicoline, &c.; and the effects of these substances were compared with those produced by the members of the chinoline series and among themselves.

The following are the general conclusions arrived at:—

1. There is a marked gradation in the extent of physiological action of the members of the pyridine series of bases, but it remains of the same kind. The lethal dose becomes reduced as we rise from the lower to the higher.

2. The higher members of the pyridine series resemble in physiological action the lower members of the chinoline series, except (1) that the

former are more liable to cause death by asphyxia, and (2) that the lethal dose of the pyridines is less than one half that of the chinolines.

3. In proceeding from the lower to the higher members of the chinoline series, the physiological action changes in character, inasmuch as the lower members appear to act chiefly on the sensory centres of the encephalon and the reflex centres of the cord, destroying the power of voluntary or reflex movement; while the higher act less on these centres, and chiefly on the motor centres, first, as irritants, causing violent convulsions, and at length producing complete paralysis. At the same time, while the reflex activity of the centres in the spinal cord appear to be inactive, they may be readily roused to action by strychnine.

4. On comparing the action of such compounds as C_9H_7N (chinoline) with $C_9H_{13}N$ (parvoline &c.), or $C_8H_{11}N$ (collidine) with $C_8H_{15}N$ (conia, from hemlock), or $C_{10}H_{10}N_2$ (dipyridine) with $C_{10}H_{14}N_2$ (nicotine, from tobacco), it is to be observed that the physiological activity of the substance is, apart from chemical structure, greatest in those bases containing the larger amount of hydrogen.

5. Those artificial bases which approximate the percentage composition of natural bases are much weaker physiologically, so far as can be estimated by amount of dose, than the natural bases; but the *kind* of action is the same in both cases.

6. When the bases of the pyridine series are doubled by condensation, producing dipyridine, parapicoline, &c., they not only become more active physiologically, but the action differs in kind from that of the simple bases, and resembles the action of natural bases or alkaloids having a similar chemical constitution.

7. All the substances examined in this research are remarkable for not possessing any specific paralytic action on the heart likely to cause syncope; but they destroy life either by exhaustive convulsions, or by gradual paralysis of the centres of respiration, thus causing asphyxia.

8. There is no appreciable immediate action on the sympathetic system of nerves. There is probably a secondary action, because after large doses the vasomotor centre, in common with other centres, becomes involved.

9. There is no difference, so far as could be discovered, between the physiological action of bases obtained from cinchonine and those derived from tar.